

FINAL REPORT

EVALUATION OF LONG ACTING NEUROLEPTICS TO
DECREASE HANDLING STRESS IN WAPITI

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FINAL REPORT FOR PROJECT 98000006

**“EVALUATION OF ZUCLOPENTHIXOL ACETATE TO
DECREASE HANDLING STRESS IN WAPITI”**

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Abstract/Summary

Handling stress and capture myopathy are important consequences of intensively managing wildlife species. As alternate livestock industries continue to grow and profit in Canada, there is an increasing need to develop methods to minimize the risks of handling these species to the animals and to the producers. Over the last 20 years, the use of long-acting neuroleptics (LAN's) in wildlife has grown, and these drugs have been found to be a valuable tool in decreasing capture and handling stress in many species. At this time, their reported use in North American species is limited. The major objective of this study was to evaluate the use of one LAN – zuclopenthixol acetate (Clopixol-Acuphase[®]) in wapiti (*Cervus elaphus*), and to assess its use as a means to decrease both quantifiable and subjective measurements of stress in this species. Eleven animals randomly received this drug and 12 animals acted as controls. There was a measurable and significant decrease in stress and activity while in the handling chute for the treated animals. The peak effects of the drug appeared on the day following drug administration, and measurable effects were still apparent on the third day. The results of this study support the use of Clopixol-Acuphase[®] in wapiti as a means to decrease handling stress. Further study is indicated to evaluate its use during other potentially stressful periods in this species (i.e. transportation, velveting) as well as in other North American species.

Executive Summary

The major objective of this project was to evaluate the use of zuclopenthixol acetate (Clompixol-Acuphase^R) to decrease handling stress in wapiti (*Cervus elaphus*). There is an increasing need to facilitate the management of this species while minimizing stress and injury to animals and producers. The worldwide use of long-acting neuroleptics in many wild ungulates has been well documented over the last 20 years, while their use in Canada has been limited. We chose to evaluate this particular drug for several reasons. It has been used with success in many other species, and approximate dose ranges are known. It is available for extra-label use by veterinarians in Canada, and is formulated for intramuscular administration. In addition, its duration of effect has been found to be approximately 3 days which we felt would be a useful duration to facilitate many procedures performed on this species in captivity. The fieldwork for this project was performed in February of 1999 using wild wapiti from the Duck Mountains and Interlake regions of Manitoba. These animals had been caught over the previous month by the Manitoba Department of Agriculture for other purposes. We performed the research over a one-week period, and the project went very well with only minor technical difficulties.

Animals which received the drug were found to be less excited based on subjective observations. These animals were observed to spend more time lying down, feeding, and performing normal grooming behavior during the study period than were the control animals. Physiological parameters measured over the study were also significantly different between groups. The control animals had elevated body temperatures during handling. These animals also showed elevations in serum cortisol levels and were more hemoconcentrated, both of which suggest increased physiologic stress. The control animals were also more active during handling, and blood parameters reflected this in elevated blood lactate levels and greater degrees of acidosis. Finally, the only animals found to have evidence of extreme muscular injury based on serum biochemistry were control animals. The peak effects of the drug appeared one day after administration, and it still appeared to be active three days after administration although its effects were waning.

All of the animals survived the study and there were no major complications. We are very pleased with the results, and are excited about their implications for the use of Clopixol-Acuphase^R in this species.

Technical Report

EVALUATION OF ZUCLOPENTHIXOL ACETATE TO DECREASE HANDLING STRESS IN WAPITI (*Cervus elaphus*)

Background

With the continued worldwide development of game farming and wildlife management techniques in recent years, there has been a concurrent increase in the public's concern that the well-being of these animals be protected.¹ It has long been assumed that measuring "stress" in these animals would provide an indication of well-being. Difficulties arise when attempting to measure stress in animals, since there is no well-defined definition of stress, and even more poorly defined parameters to measure it. Traditionally, increased plasma levels of corticosteroids have been used as a measure of stress, however the adrenal cortical response does not always occur, suggesting an over-reliance on this parameter as a measure of stress. When an animal is confronted with a potentially stressful situation, it relies on 3 biological systems to cope: behavior, the autonomic nervous system, and the neuroendocrine system.¹ For this reason, measurement of several variables, as well as making subjective assessments of behavior and activity, should give more reliable estimates of stress.^{1,2}

Capture myopathy is a serious and potentially fatal consequence of capturing and handling wild animals. This syndrome is characterized by varying degrees of homeostatic imbalances resulting from increased muscular activity, autonomic nervous system discharge, and physical injury.⁴ As a result of the increased muscular activity associated with capture and handling, body temperature is elevated, muscle damage may result in leakage of enzymes, and anaerobic activity contributes to lactic acidosis. Depending on the degree of activity and the individual animal's ability to compensate for the changes, the syndrome may manifest as shock, myopathy, renal failure, rupture of muscle bodies, and sudden death.⁴ In terms of measuring stress variables other than plasma cortisol, measuring body temperature, blood lactate, acid-base balance, heart rate, respiratory rate, and serum biochemistry may be more helpful in determining the effects

of increased activity during handling and susceptibility of the animal to capture myopathy.

One method of decreasing the incidence of stress, injuries, and mortalities in wild animals is the use of neuroleptics or tranquilizers.⁵ These drugs are used to alleviate anxiety, have prolonged durations of action, and have few side effects when used properly. Beneficial effects include: general calming effect, indifference to new and unnatural surroundings, loss of fear of humans, and reductions in aggressive behavior.⁵ These agents have been used successfully around the world in the management of many wild herbivores, but there are few reports of their use in North American species.⁵

This study was designed to evaluate the use of zuclopenthixol acetate (Clopixol-Acuphase^R, Lundbeck, Canada) to decrease handling stress in wild wapiti (*Cervus elaphus*). This injectable neuroleptic was developed for use in the management of acute psychoses in human patients that refused to take oral neuroleptics in the initial stages of their treatment.⁶ This formulation of zuclopenthixol acetate is dissolved in a thin vegetable oil which permits slow release of drug from the intramuscular site of administration, prolonging the duration of its clinical effect. This drug has been evaluated previously in farmed red deer in Scotland, and benefits of its use in decreasing stress were found.^{7,8,9}

We planned to measure several physiological variables in order to characterize stress and activity of wild wapiti during handling. The study protocol was designed to collect data on temperature, heart rate, respiratory rate, complete blood count, serum biochemistry, serum cortisol, blood lactate, venous blood gas status, and subjective stress and activity assessment. By measuring this broad range of parameters, we would be able to better characterize the stress of handling, and to determine any benefit from treatment with zuclopenthixol acetate.

Materials and Methods

Background: In order to establish a captive population of native wapiti for game-farming purposes in Manitoba, Canada, over 200 animals were captured in January and February, 1999. These animals were captured by baiting them with food into large pens, and they were then transported by trailer to a holding facility. The elk were captured in

the Duck Mountains (NE15-33-29, SE9-33-29) and Interlake region (SE20-21-3W) of Manitoba. Processing of animals at the time of capture included marking with Manitoba Government unique ear tags and Health of Animal ear tags, testing for tuberculosis and brucellosis, collecting blood samples for DNA genotyping, collecting fecal samples for analysis, treating with an ectoparasiticide, and vaccination with 8-way clostridial vaccine. All animals tested negative for tuberculosis and brucellosis.

For the purposes of the study reported here, 23 male elk aged 1-2 years were separated and maintained at a holding facility in Grunthal, Manitoba. These animals were selected for the study in order to prevent imposing stress associated with the research on pregnant animals, and for the ease of maintaining subadult males together. The study took place in February, 1999 with daily temperatures ranging from -5 to $+4^{\circ}\text{C}$. It was approved by the University of Saskatchewan Animal Care Committee and regional alternate livestock associations, and was conducted with the cooperation of the Manitoba Department of Agriculture.

Study Protocol : On the first day of the study (Day 1), individual animals were moved through chutes (NV Elk Modular Handling System, Bateman, Saskatchewan, Canada) and held in a hydraulic squeeze chute (Kiwi Elk Systems, Wildwood, Alberta, Canada) for physiologic data collection. Each animal was randomly assigned to a treatment group by flipping a coin prior to processing, and the primary investigator was blinded to the treatment. Once secure in the squeeze and blindfolded, respiratory rate was measured by auscultation over the trachea, and heart rate was measured by auscultation over the heart. To minimize time in the chute, rates were measured over 15 seconds each, then converted to rates per minute. The hair was clipped over the jugular furrow, and blood was collected from the jugular vein into serum separator tubes for serum cortisol and biochemical analysis, and into an EDTA tube for measurement of complete blood count. Free-flowing venous blood was collected anaerobically into a heparinized syringe for venous blood gas analysis and blood lactate analysis. Rectal temperature was measured with a digital thermometer.

At the completion of data collection, the body weight was estimated and the animal received either 1mg/kg estimated body weight of zuclopenthixol acetate or an equal volume of saline injected intramuscularly into the muscles of the hindlimb. The animal

was marked with livestock paint as to the treatment group ("X" or "O") and was released into a pen based on its treatment. The total time in the chute was recorded to the nearest 30 seconds. A subjective assessment of stress was assigned to the animal by the primary investigator based on ease of handling and excitement in the squeeze (1 – mild excitement and struggle, 2- moderate excitement and struggle, 3- marked excitement and struggle).

On Day 2, animals were processed for data collection according to their group (i.e. for ease of handling, all animals of one group were processed before those of the other group). Once in the chute, an electronic scale (Eziweigh 2, Tru-test Ltd., Auckland, New Zealand) was used to determine actual body weight. All physiologic measurements were taken as before, and the animals were released back into their separate pens.

On Day 4, animals were again processed for data collection in the same order as before.

Prior to data collection each day, treatment groups were observed for 5 minutes to determine a rough estimate of flight distance and activity level when approached by a person.

Laboratory Analysis : Blood samples for serum cortisol and biochemical analysis were allowed to clot at room temperature, were centrifuged and placed on ice. Blood smears were made from the heparinized samples immediately after collection and allowed to dry, and the EDTA tubes were placed on ice. Blood samples were analyzed within 24 hours. Serum biochemistry profiles were performed by a Vitros Ektachem 700, and serum cortisol levels were determined by an Immulite 2000 using chemiluminescence immunoassay. Complete blood cell profiles were performed by a Coulter S770 using EDTA samples together with manual methods for determination of white blood cell differential count. Blood lactate was measured immediately after collection using a portable analyzer (Accusport Portable Lactate Analyzer, Boehringer Mannheim Corporation, Indianapolis, IN, USA). On days 1 and 2, venous blood gas samples were analyzed immediately after collection using a portable analyzer (i-STAT Portable Clinical Analyzer, i-STAT Corporation, East Windsor, NJ, USA). Due to technical difficulties with the portable analyzer on Day 4, samples were put into ice water and analyzed using a separate blood gas analyzer (ABL520, Radiometer, Copenhagen, Denmark) in a laboratory within 3 hours.

Statistical Analysis : Statistical analysis was performed using Statistix (Student's Edition of Statistix, Version 1.0, Analytical Software). Data collected were first analyzed for normalcy. Based on the normalized results, mean data from each treatment group were analyzed for same-day differences using a 2-sample t-test. Mean data were then analyzed for differences between days for the same treatment group using a paired t-test. The null hypothesis was that there were no differences between the means for the two groups compared in each test. Statistical significance was set with $p < 0.05$.

Results

There were no mortalities, and all animals were included in the analysis. There was no difference in handling times in the chute between the two treatment groups on any day.

Data collected from Day 1 showed no statistical significance in differences between means of treatment groups for any measured variables using a two sample t-test. All animals had similar physiological responses to the imposed stress of handling in the chute. Selected mean values were pooled, and are shown in Table 1.

Within hours of drug administration on Day 1, treated animals subjectively appeared calm and their activity levels were decreased.

Table 1. Mean values ($\pm$ SD) for wild elk prior to treatment with zuclopenthixol acetate (Clopixol-Acuphase^R) or saline placebo. There is no statistically significant difference between groups based on 2-sample t-test.

Variable	Clopixol Treatment (n=11)	Saline Treatment (n=12)
Temperature ($^{\circ}$ C)	40.93 ($\pm$ 0.94)	41.22 ($\pm$ 0.97)
Heart Rate (#/minute)	84.82 ($\pm$ 22.90)	87.83 ($\pm$ 29.82)
Respiratory Rate (#/minute)	32.36 ($\pm$ 18.10)	36.83 ($\pm$ 20.32)
pH _v	7.30 ($\pm$ 0.05)	7.30 ($\pm$ 0.06)
HCO ₃ ⁻ (mmol/L)	23.91 ($\pm$ 4.06)	23.92 ($\pm$ 4.30)
BE (mmol/L)	-1.55 ($\pm$ 4.13)	-1.42 ($\pm$ 4.87)
Blood lactate (mmol/L)	7.57 ($\pm$ 1.96)	7.47 ($\pm$ 2.56)
Serum cortisol (mmol/L)	108.91 ($\pm$ 24.56)	125.42 ($\pm$ 37.89)
TP (g/L)	68.64 ($\pm$ 4.37)	67.58 ($\pm$ 6.61)
RBC ($\times 10^{12}$ /L)	10.51 ($\pm$ 0.91)	10.40 ($\pm$ 0.87)
PCV (L/L)	0.49 ($\pm$ 0.04)	0.49 ($\pm$ 0.04)
HgB (g/L)	176.36 ($\pm$ 11.21)	178.33 ($\pm$ 10.25)
WBC ($\times 10^9$ /L)	5.45 ($\pm$ 1.46)	5.28 ($\pm$ 2.00)
Lymphs ($\times 10^9$ /L)	2.22 ($\pm$ 0.61)	2.30 ($\pm$ 0.64)

Data from Day 2 (~24 hours after treatment) showed statistically significant differences with a two sample t-test in several variables. These variables and their mean values are presented in Table 2.

Table 2. Mean values (+/- SD) for wild elk 24 hours after treatment with zuclopenthixol acetate (Clopixol-Acuphase^R) or saline placebo. Values reported are those that show statistical significance ($p < 0.05$) in difference between treatment groups.

Variable	Clopixol Treatment (n=11)	Saline Treatment (n=12)	p value
Temperature (°C)	39.00 (+/- 0.40)	40.63 (+/- 0.60)	<0.0001
pH _v	7.45 (+/- 0.02)	7.34 (+/- 0.03)	<0.0001
HCO ₃ ⁻ (mmol/L)	29.36 (+/- 2.66)	24.25 (+/- 3.11)	0.0004
BE (mmol/L)	5.64 (+/- 2.94)	-0.83 (+/- 3.56)	0.0001
Blood lactate (mmol/L)	3.39 (+/- 1.17)	5.98 (+/- 1.49)	0.0002
Serum cortisol (mmol/L)	97.91 (+/- 28.98)	139.50 (+/- 44.12)	0.0151
TP (g/L)	65.00 (+/- 4.54)	70.25 (+/- 6.50)	0.0371
RBC (x10 ¹² /L)	9.19 (+/- 0.78)	10.43 (+/- 0.92)	0.0023
PCV (L/L)	0.42 (+/- 0.04)	0.49 (+/- 0.03)	0.0001
HgB (g/L)	159.09 (+/- 11.37)	181.75 (+/- 7.02)	<0.0001
WBC (x10 ⁹ /L)	5.55 (+/- 1.68)	7.33 (+/- 1.89)	0.0271
Lymphs (x10 ⁹ /L)	1.43 (+/- 0.47)	2.41 (+/- 0.44)	<0.0001

Although not statistically significant, the mean respiratory rate of the treated animals was 20, while that of the control animals was 41. There was no significant difference in mean heart rate (72.7 bpm vs. 70.2 bpm), serum glucose (9.5 mmol/L vs. 10.1 mmol/L), urea (10.8 mmol/L vs. 11.0 mmol/L) or creatinine (134.7 mmol/L vs. 147.8 mmol/L) between treatment and control animals.

Data from Day 4 (~72 hours after treatment) also showed statistically significant differences using a two sample t-test in several variables. These variables and their mean values (+/- SD) are presented in Table 3.

Table 3. Mean values (+/- SD) for wild elk 72 hours after treatment with zuclopenthixol acetate (Clopixol-Acuphase^R) or saline placebo. Values reported are all those that show statistical significance ($p < 0.05$) in difference between treatment groups.

Variable	Clopixol Treatment n=11)	Saline Treatment (n=12)	p value
Serum cortisol (mmol/L)	92.82	135.92	0.0074
PCV (L/L)	0.45	0.50	0.0086
HgB (g/L)	167.55	179.00	0.0087

Significant differences were still present 72 hours after drug treatment in three hematological variables. Treated animals had lower mean serum cortisol (92.82mmol/L vs. 135.92mmol/L), PCV (0.45L/L vs. 0.50L/L), and hemoglobin (167.55g/L vs. 179.0g/L) than did control animals. Other measured variables showed no significant difference of mean values between groups on Day 4.

Interestingly, the mean values for the treated animals rose between Day 2 and Day 4 to approach those values of the control animals on Day 4.

Paired t-tests were also performed on data from each treatment group alone to compare variables between days of data collection (Day 1 vs. Day 2, Day 1 vs. Day 4). Significance was determined for many variables for each treatment group on each pair of days. The paired t-tests (data not shown) suggest that over the study period there was acclimatization of all animals to the handling process, and that the treated animals appeared to accommodate sooner (Day 2 vs. Day 4) based on comparing many of their parameters with those of the control animals.

Although not showing statistical difference between treatment groups, the only animals that were found to have markedly elevated CPK and AST values were control animals. The data collected from Day 2 suggests that two control animals had marked, subclinical muscle injury (CPK = 42080U/L, 25887U/L, and AST = 1387U/L, 696U/L) at the time of blood sampling. These animals were not observed to be lame, and appeared no different from their pen-mates.

Subjective stress assessments for the animals over the study period found that treated animals were easier to handle on Day 2 than controls. By Day 4, this effect was not as apparent as all animals appeared to be accommodating to the handling process.

On observation prior to handling on Day 2, treated animals had less activity (circling, pacing) in their pen and showed less excitement when approached by a person. Control animals were much more active in their pen, and became excited and attempted to escape when approached by a person. Flight distance could not be accurately estimated for either group.

On Day 4, the subjective assessment of activity was more difficult to make since differences between groups were not as apparent.

Discussion

Although not the main purpose of this research, valuable data was collected from these wapiti in terms of hematological and physical parameters. The consistency of sampling technique used in the study provided us with information which can be used by others when assessing wapiti physiological variables.

The information collected on Day 1 provides us with a strong database for restrained, wild male wapiti. During handling, these animals showed marked excitement and activity in the chute.

When attempting to assess "stress" in an animal, it is possible to examine the three systems that the animal uses to cope with the disruption to its homeostasis: behavior, the autonomic nervous system, and the neuroendocrine system.¹ Behavioral changes are often difficult to measure, and are frequently restricted to subjective assessment of abnormal behaviors such as aggression and attempts to escape confinement. The wapiti in this study showed marked excitement and struggle on the first handling, but there was a noticeable decrease in the treated animals on the second day. These animals were easier to move through the handling facility and stood quietly in the squeeze chute during data collection. By the fourth day, the subjective assessment was not as apparent, as both groups of animals were easier to handle, suggesting that the animals were acclimatizing to the handling process.

Since autonomic nervous system activation alters cardiopulmonary status, the end points of heart rate and respiratory rate have been used to study stress.¹ In this study, there was no significant difference in these parameters between treatment groups on any of the days. This suggests that these variables may not be adequate as the sole determinants of stress in this species. This shows the importance of measuring several variables to give a more reliable measurement of stress,² and also emphasizes that investigators should look for end points that have a meaningful impact on the animal's well-being.¹ In anticipation of this, we planned to measure variables which would reflect the hematological, biochemical, and acid-base status of the animals in order to determine predisposition to, and prevention of capture myopathy-type processes.

The benefits of using zuclopenthixol acetate (ZPTA) in these wapiti is most apparent when comparing animals 24 hours after drug administration. The mean temperature was 1.6°C less in treated animals, suggesting less muscular activity during handling. Rectal temperature is a reliable indicator of excitement and increased muscular activity, and has been used to evaluate stress in other species.^{10,11}

Hematological variables have been shown to provide valuable information for stress assessment in many species.¹²⁻¹⁹ The ZPTA treated group had lower red blood cell count, packed cell volume, hemoglobin, and total serum protein than the control group on Day 2, and showed a similar trend on Day 4. With activation of the autonomic nervous system, there is a release of catecholamines from the adrenal medulla. These hormones cause splenic contraction, resulting in more red blood cells in circulation to potentially increase oxygen delivery to depleted tissues during the stressful event. The resulting hemoconcentration is measured as increased red cell mass, and has been seen in many species.¹²⁻¹⁹ In addition, studies have shown a greater degree of hemoconcentration in manually restrained animals than in chemically immobilized animals, suggesting that manual restraint is more stressful to the animal than the capture process itself.^{13,15,19} The significant reduction in hemoconcentration in the ZPTA treated animals is suggestive of less splenic contraction, resulting from less sympathetic stimulation from stress. Since all animals showed similar hematological profiles on Day 1, this decrease in red cell mass on Day 2 and Day 4 is due to the effectiveness of the ZPTA in decreasing the stress response in treated animals.

A contributing factor to the greater degree of hemoconcentration in the control group could be mild dehydration. This group was observed to spend less time performing normal behaviors such as eating and drinking, and this could be reflected in these measurements as has been reported previously in elk.¹⁸ Serum urea and creatinine levels were not significantly different between groups.

ZPTA treated animals also had a significantly lower white blood cell count and absolute lymphocyte count than the controls. Catecholamine release during the initial alarm phase may result in neutrophilia and lymphocytosis, while the release of corticosteroids from the adrenal gland in response to more chronic stress may cause a decrease in lymphocyte count.¹² Although no significant difference existed for segmented neutrophil counts

between groups, the ZPTA treated animals had fewer lymphocytes. This may reflect blood sampling in the acute phase of the stress response, when catecholamine effects on lymphocyte dynamics in circulation predominate over cortisol effects. Control animals were more stressed during handling, and could therefore be expected to have more lymphocytes in circulation at this time. These findings contrast previous reports in elk, which describe higher neutrophil than lymphocyte counts.^{17,18} This could be due to sampling at a later phase of the stress response, when cortisol effects on white blood cells dominate, causing neutrophilia and lymphopenia.¹²

Serum biochemical profiles showed little significant difference between groups. There were no differences in serum urea, creatinine or muscle enzyme levels. Although not statistically significant, the only animals to have marked elevations in the muscle enzymes CPK and AST were control animals. Two control animals in this study showed elevations on Day 2 with CPK values of 42,080 U/L and 25,887 U/L which is consistent with muscle injury within the last 24 hours. Severe muscle damage in red deer has been reported to cause elevations of CPK to 35-47,500 U/L.²⁰ It is interesting that these two animals showed no signs of injury, however it was reported that in white-tailed deer, 10- to 200-fold increases in CPK values occurred approximately 24 hours after handling, without overt signs of external damage or altered behavior of the affected animals.²¹

Blood gas values show great promise in assessing activity during handling. The increased struggle and muscular activity of stressed animals leads to anaerobic metabolism for energy production.⁴ This process generates large amounts of lactic acid, which dissociates to form lactate and hydrogen ions. The rise in hydrogen ions overwhelms the buffering capacity in the body, and the animal becomes acidotic.²² The recent development of portable blood-gas analyzers and lactate analyzers provides the opportunity to measure these variables in the field and to assess the degree of anaerobic metabolism, the ability of the animal to compensate, and the degree of imbalance. Venous blood gas analysis of free-flowing (vein not occluded during sampling) jugular samples can provide a measure of blood flow, oxygen delivery, clearance of carbon dioxide, and acid-base balance. Activity and exertion are important contributing factors to capture myopathy, and our ability to characterize them will continue to develop in the future.

The control animals had blood gas values that were much more suggestive of metabolic acidosis than those from the ZPTA treated animals. There was significant differences in venous blood pH, bicarbonate, and base excess between the two groups. The most likely cause was the increased activity and anaerobic cellular metabolism in the control animals. Together with the significantly increased blood lactate values in the control animals, it is likely that they had developed lactic acidosis during the handling process. The ZPTA treated animals had approximately 40% lower blood lactate levels than the controls. The findings from the control group are similar to, though not as impressive as reported blood gas values from bighorn sheep after pursuit and capture which showed marked metabolic acidosis.²³

To our knowledge, this is the first report of measuring blood lactate levels in free-ranging wildlife. Blood lactate has been studied previously as a measure of stress.²⁴ Apple *et al.* (1993) studied the effects of stress in sheep by separating individual animals from the flock and performing repeated restraint for blood collection. They found significant increases in plasma lactate of greater than double the values from controls due to this repeated stressor.²⁴

The presence of lactic acidosis is suggestive of increased anaerobic metabolism, and has been reported most often in cases of general circulatory failure, especially in the later stages.²² In this study, the ZPTA treated animals had significantly lower blood lactate levels which reflects less anaerobic activity and stress during handling. More investigation is warranted to determine prognostic levels of blood lactate in this species, and levels present in cases of capture myopathy. It should also be noted that blood lactate levels are most useful when serially measured over time and during treatment in order to establish trends, so drawing conclusions from the single samples in this study should be done with caution.

This study also assessed the "classic" measure of stress by measuring serum cortisol levels. There was significant difference between ZPTA treated animals and controls, with treated animals having a 30% reduction in the level of cortisol. Although serum cortisol should not be used as the only determinant of stress, it has been found to be useful in a number of species.^{15,25,26} Serum cortisol levels in white-tailed deer and moose

reflected the degree of excitement during capture and restraint, and agreed well with subjective visual evaluation of handling stress.^{25,26}

By measuring a variety of physiological variables, we were able to characterize the stress response to handling in wild wapiti. The use of zuclopenthixol acetate in this species was shown to be very effective in decreasing the stress response. Treated animals were easier to handle, showed lower rectal temperatures, less hemoconcentration, less lactic acidosis, lower incidence of elevated muscle enzymes, and lower serum cortisol levels. The drug was effective within 24 hours of administration, and its effects were measurable but waning by 72 hours. This drug shows great potential for use in this species, and its use in other periods of stress (transportation, velveting) should be evaluated. It also has potential for use in other native species, and further research is warranted to evaluate its use in other intensively farmed and managed species.

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